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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/466,568	12/17/1999	GERALD R. CRABTREE	APBI-P16-316	1333

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ROPES & GRAY  
ONE INTERNATIONAL PLACE  
BOSTON, MA 02110-2624

EXAMINER

LOEB, BRONWEN

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 11/05/2002

24

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/466,568

Applicant(s)

CRABTREE ET AL.

Examiner

Bronwen M. Loeb

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 Nov. 2001 & 12 Aug 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 14, 17, 18, 22-24, 30, 32, 33 and 48-69 is/are pending in the application.
- 4a) Of the above claim(s) 17, 24, 30, 32, 33 and 48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14, 18, 22, 23 and 49-69 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 December 1999 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: See Continuation Sheet.

Continuation of Attachment(s) 6). Other: Copy of Papers Originally Filed information.

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The following papers have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process:

Mailroom Stamp Date

Certificate of Mailing Date

26 June 2002

19 June 2002

Paper 25

12 August 2002

7 August 2002

Papers #24-28

The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

COPY OF PAPERS  
ORIGINALLY FILED

If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will, **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.

Part of Paper No. 29

### **DETAILED ACTION**

This action is in response to the amendments filed 26 November 2001, in which claims 14, 18, 22 and 23 were amended, claims 1, 6, 20, 31, 36-39 and 45 were cancelled and new claims 49-69 were presented, and 12 August 2002, in which amendments to the specification were made.

It is noted that in the amendment filed 26 November 2001 on p. 9, Applicant states that non-elected claims have been cancelled. No record of such claim cancellation is found in the file. Thus, the non-elected claims (claims 17, 24, 30, 32, 33 and 48) remain pending.

Claims 14, 17, 22-24, 30, 32, 33 and 48-69 are pending.

### ***Election/Restrictions***

1. Claims 17, 24, 30, 32, 33 and 48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

### ***Sequence Compliance***

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences were set forth that lack sequence identifiers, no computer readable format (CRF) was filed, no paper sequence was filed and no attorney statement was filed. These sequences include **the PEST sequence on page 21, line 31**. If the Sequence Listing required for the instant application is identical to that of another application, a letter may be submitted requesting transfer of

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the previously filed sequence information to the instant application. For a sample letter requesting transfer of sequence information, refer to MPEP § 2422.05. Additionally, it is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP § 2422.02).

Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

#### ***Information Disclosure Statement***

1. The information disclosure statement (IDS) filed 26 June 2002 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it lacks a copy of each cited reference. It is stated that no copies were filed "because the citations were made in prior application U.S.S.N. 08/605,578, filed February 22, 1996 which is relied upon for an earlier filing date under 35 USC §120". First, case 08/605,578 does not contain any of the references cited on the PTO-1449 submitted. Second, it is noted that 08/605,578 is not claimed as a priority document in this case (for instance, see the amendment to the specification filed 26 November 2001). The IDS has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining

compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

### ***Specification***

3. The amendment filed 27 August 2002 is objected to under 35 U.S.C. §132 because it introduces new matter into the disclosure. 35 U.S.C. §132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendment to p. 1 of the specification filed 26 November 2001 includes the following: "The contents of each of these applications is hereby incorporated by reference into the present disclosure. The full contents of related cases PCT/US94/01617, PCT/US94/01660 and PCT/US94/08008 are also incorporated by reference into the present disclosure". This is new matter as the as-filed specification did not contain such a statement of incorporation.

Applicant is required to cancel the new matter in the reply to this Office Action.

4. The disclosure remains objected to because of the following informalities: The abbreviations used in Figure 15 are not defined in the corresponding Brief Description of the Drawings: DAG, PKC, PLC $\gamma$ 1, NFAT<sub>C</sub> and NFAT<sub>N</sub>. On p. 50, line 28, the cited figure should be Fig. 6A, not "Fig. 6". On p. 49, line 29, an unknown abbreviation "TAC" is recited. Pages 45, 47 and 57 contain what appear to be handwritten amendments to the specification.

Appropriate correction is required.

***Response to Amendment***

5. All rejections of claims 1, 6, 20, 21, 31, 36-39 and 45 have been withdrawn in view of Applicant's amendment canceling these claims.

The rejection of claims 14, 18, 22 and 23 under 35 U.S.C. §112, second paragraph, as being indefinite has been withdrawn in view of Applicant's amendment. It is noted that with respect to claim 18, the word "contain" has been examined assuming open claim language (i.e. comprise). Similarly new claim 64 which recites "containing" has been examined assuming open claim language (i.e. comprising).

The rejection of claim 18 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-76 of U.S. Patent No. 6,140,120 has been withdrawn in view of Applicant's amendment.

The rejection of claim 14 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-127 of U.S. Patent No. 6,046,047 has been withdrawn in view of Applicant's amendment.

The provisional rejection of claim 18 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 44-54 of copending Application No. 09/582,916 has been withdrawn in view of Applicant's amendment.



The rejection of claim 18 as being not patentably distinct from claims 4 and 10 of commonly assigned USP 6,117,680 has been withdrawn in view of Applicant's amendment.

The rejection of claims 18 and 22 under 35 U.S.C. §102(b) as being anticipated by Spencer et al (1993 Science 262: 1019-1024) has been withdrawn in view of Applicant's amendment.

The rejection of claims 14, 18, 22 and 23 under 35 U.S.C. §102(b) as being anticipated by Young et al (WO 95/34646) has been withdrawn in view of Applicant's amendment.

The rejection of claims 14, 18, 22 and 23 under 35 U.S.C. §102(b) as being anticipated by Crabtree et al (USP 5,834,266) has been withdrawn in view of Applicant's amendment.

The rejection of claims 14, 18, 22 and 23 rejected under 35 U.S.C. §102(e) as being anticipated by Liu et al (USP 5,928,868) has been withdrawn in view of Applicant's amendment.

The rejection of claims 14, 18, 22 and 23 under 35 U.S.C. §102(b) as being anticipated by Rivera et al (Nature Medicine (1996) 2:1028-1032) has been withdrawn in view of Applicant's amendment.

The rejection of claim 14 under 35 U.S.C. §102(b) as being unpatentable over Arvidsson et al (Cell Growth and Differentiation (1992) 3:881-887) has been withdrawn in view of Applicant's amendment.

The rejection of claims 22 and 23 under 35 U.S.C. §102(b) as being anticipated by Becker et al (Mol. Cell. Biol. (1989) 9:3878-3887) has been withdrawn in view of Applicant's amendment.

The rejection of claims 14, 18, 22 and 23 under 35 U.S.C. §102(e) as being anticipated by Natesan et al (USP 6,117,680) has been withdrawn in view of Applicant's amendment.

The rejection of claims 18 and 22 under 35 U.S.C. §103(a) as being unpatentable over Spencer et al has been withdrawn in view of Applicant's amendment.

The rejection of claims 14 and 18 under 35 U.S.C. §103(a) as being unpatentable over Arvidsson et al has been withdrawn in view of Applicant's amendment.

6. Claim 18 stands rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 62-129 of U.S. Patent No. 6,165,787 for reasons of record and as further discussed below.

Claims 23 and new claims 50-53 and 65-69, stand under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-71 of U.S. Patent No. 6,043,082 for reasons of record and as further discussed below.

Claims 18 and 23, and amended claim 22, stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 87-142 and 154-162 of U.S. Patent No. 5,869,337 for reasons of record and as further discussed below.

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Claims 14, 18, and new claim 64, stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 72-202 of U.S. Patent No. 5,834,266 for reasons of record and as further discussed below.

Claims 18 and amended claims 14 and 22 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14-28, 37, 38, 40, 43-52 and 60-62 of U.S. Patent No. 6,117,680 for reasons of record and as further discussed below.

Claim 18 and amended claim 23 and new claim 52, stand rejected under 35 U.S.C. §102(b) as being anticipated by Arvidsson et al (Cell Growth and Differentiation 1992 3:881-887) for reasons of record and as further discussed below.

7. New grounds of rejection, necessitated by Applicant's amendment, are presented below.

### ***Response to Arguments***

8. With regard to the various obviousness-type double patenting rejections, Applicant states that Applicant will submit a terminal disclaimer, if necessary, upon indication of allowable subject matter. Only those rejections have been maintained in which the amended claims are obvious in view of allowed claims.

9. With regard to the rejection of claim 18, amended claim 23 and new claim 52, under 35 U.S.C. §102(b) as being anticipated by Arvidsson et al, Applicant's arguments have been fully considered but are deemed not persuasive.

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Applicant has amended claim 18. This amendment however does not overcome the rejection. Furthermore, amended claim 23 and new claim 52 are now anticipated by Arvidsson et al.

Arvidsson et al teach genetic constructs comprising chimeric PDGF receptors, which comprise a ligand-binding domain for PDGF, a transmembrane domain (thus a membrane retention domain) and a signaling domain that induces mitogenicity in the cells. PDGF binds and dimerizes its receptor thus inducing activity of the signaling domain. These constructs anticipate claim 23. The constructs were expressed in porcine aortic endothelial cells, thus anticipating claim 18. The transmembrane domain is a membrane retention domain, thus anticipating claim 52. See abstract.

### **New Grounds of Rejection**

#### **Claim Rejections - 35 USC § 112**

10. The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 55, 56, 61, 62, 66 and 67 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is based on the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, first paragraph "Written Description" Requirement published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claims 55, 61 and 66 are drawn to a composition wherein the ligand-binding domain of at least one of the chimeric proteins is a variant of an FKBP domain. This is a genus claim in terms of any variant of an FKBP domain. Claims 56, 62 and 67 are drawn to a composition wherein at least one of the ligand-binding domains comprises FKBP12 or a variant thereof in which one or more of Tyr26, Phe36, Asp37, Tyr82 and Phe99 are replaced by other amino acids. This is a genus claim in terms of any variant of an FKBP12 in which one or more of Tyr26, Phe36, Asp37, Tyr82 and Phe99 are replaced by other amino acids. The specification mentions FKBP12 mutants at Tyr 26, Phe36, Asp37, Tyr 83 and Phe99. This disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all variants based on the teachings in the specification. The specification lacks a definition of what a variant is thus the broadest interpretation is that it encompasses any mutant of an FKBP domain which includes truncations, substitutions, insertions and internal deletions. There is little to no discussion in the specification of relationship between the FKBP primary sequence and its function (see bridge, pp. 28-29). While there is what appears to be a structure-function relationship disclosed between specific amino acids and the binding pocket of the FKBP domain, there is no disclosure of the amino acids that form the hydrophobic core of the protein and which are therefore essential to the proper folding of the domain.

There is also no disclosure of what amino acids could be deleted or where insertions could be made and maintain the structure and function of the FKBP domain. Therefore, the specification does not describe the claimed FKBP variants in such full, clear, concise and exact terms so as to indicate that Applicant has possession of these variants at the time of filing the present application. Thus, the written description requirement has not been satisfied.

12. The following is a quotation of the second paragraph of 35 U.S.C. §112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 14, 18, 22, 23 and 49-69 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is vague and indefinite in its (b) recitation. It is unclear what makes the second chimeric protein chimeric as there is no indication that one domain is heterologous thereto (as is recited in the (a) part).

Claim 23 is vague and indefinite in its (b) recitation. It is unclear what makes the second chimeric protein chimeric as there is no indication that one domain is heterologous thereto (as is recited in the (a) part).

Claim 23 is vague and indefinite in reciting "a ligand binding domain of the first chimeric protein" in line 3 of step (b). Is this ligand binding domain different from that recited in step (a)?

Claim 49 is vague and indefinite in its (b) recitation. It is unclear what makes the the second chimeric protein chimeric (in the species where any of the domains are

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different from those recited in (a)), as there is no indication in (b) that one domain is heterologous thereto (as is recited in the (a) part).

Claims 55, 56, 61, 62, 66 and 67 are vague and indefinite in reciting “a variant” of a particular domain. This is not a term of art and is not defined in the specification therefore the metes and bounds of the claim cannot be ascertained.

Claims 57, 63 and 68 are vague and indefinite in reciting “or a derivative of either”. “Either” means one or the other of two. However this recitation comes after a group listing three members thus rendering the metes and bounds of the claims unclear.

### ***Claim Rejections - 35 USC § 102***

14. Claims 14 and 18 are rejected under 35 U.S.C. §102(b) as being anticipated by Becker et al (Mol. Cell Biol. (1989) 9:3878-3887). Becker et al teaches a CV-1 or COS-1 cell comprising a genetic construct encoding a chimeric protein comprising glucocorticoid receptor and the transcriptional activation domain of E1A. Therefore, the chimeric protein comprises a ligand-binding domain and a transcriptional activation domain, which is the same as the first nucleic acid construct recited in claim 22. CV-1 and COS-1 cells are monkey cells lines and therefore are mammalian cells. Since claim 18 recites “contains and expresses **at least one** nucleic acid construct” (emphasis added), Becker et al anticipates claim 18. The construct taught by Becker et al was part of a plasmid vector which also contained the bacterial chloramphenicol acetyltransferase which permits selection of transformed bacterial cells. Thus claim 14 is also anticipated.

***Conclusion***

Claims 14, 18, 22, 23 and 49-69 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from



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10:00 AM to 6:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Tracey Johnson, Patent Analyst whose telephone number is (703) 305-2982.

Customer service for Tech Center 1600 may be reached at (703)-308-0198.

Bronwen M. Loeb, Ph.D.  
Patent Examiner  
Art Unit 1636

October 30, 2002



**JAMES KETTER**  
**PRIMARY EXAMINER**